REMARKS

These remarks are in response to the Office Action mailed February 5, 2009. Claim 13 has been canceled without prejudice to Applicants' right to prosecute the canceled subject matter in any divisional, continuation, continuation-in-part or other application. No new matter is believed to have been introduced.

I. REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Claims 1-3, 6-11, 13-18, 24 and 41-42 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. The Office Action alleges that the term "photosensitizer" is not defined and does not address what materials, components, or compounds would fulfill the description. Applicants respectfully traverse this rejection.

The specification is incredibly clear on the what a photosensitizer encompasses as well as setting forth specific examples of compounds that can be used as photosensitizers. The Examiner is respectfully directed to the following paragraphs of the publication of the pending application (20060258629):

> [0015] The photosensitizer is any compound capable of activation by light radiation resulting in the destruction of the surrounding tissue. The photosensitizer can have an absorption spectrum of wavelengths between about 350 nm and 1200 nm. In one aspect, the photosensitizer is administered locally to the patient. In another aspect, the photosensitizer is administered parenterally to the patient.
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> …
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> [0031] As used herein, a "photosensitizer" or "photoreactive agent" is a compound or composition that is useful in photodynamic therapy. Such agents are capable of absorbing electromagnetic radiation and emitting energy sufficient to exert a therapeutic effect, e.g., the impairment or destruction of unwanted cells or tissue, or sufficient to be detected in diagnostic applications. The photodynamic therapy according to the invention can be performed using any of a number of photoactive compounds. For example, the photosensitizer can be any chemical compound that collects in one or more types of selected target tissues and, when exposed to light of a particular wavelength, absorbs the light and induces impairment or destruction of the target tissues. Virtually any chemical compound that homes to a selected target and absorbs light may be used in this invention. Preferably, the photosensitizer is nontoxic to the patient to which it is administered

and is capable of being formulated in a nontoxic composition. The photosensitizer is also preferably nontoxic in its photodegraded form. Ideal photosensitizers are characterized by a lack of toxicity to cells in the absence of the photochemical effect and are readily cleared from non-target tissues.

[0032] Any chemical compound that absorbs light may be used in the methods provided herein. Photosensitizers for use in the methods provided herein include, but are not limited to, indocyanine green, toluidine blue, prodrugs such as aminolevulinic acid, texaphyrins, benzoporphyrins, phenothiazines, phthalocyanines, porphyrins, merocyanines, psoralens, protoporphyrin, methylene blue, Rose Bengal, chlorins such as mono-L-aspartyl chlorin e6, alkyl ether analogs of chlorins, purpurins, bacteriochlorins, pheophorbides, pyropheophorbides, cationic dyes and any other agent that absorbs light in a range of about 500 to about 1100 nanometers. Photosensitizers for use in the methods provided herein are also disclosed in U.S. Pat. Nos. 6,319,273, 6,042,603, 5,913,884, 5,952,366, 5,430,051, 5,567,409, 5,942,534, and U.S. patent application Publication No. 2001/0,022,970, incorporated herein by reference.

[0033] The photosensitizer reagents for use in the methods provided herein include but are not limited to porphyrins such as PHOTOPHRIN™ (a QLT, Ltd. brand of sodium porfimer), and FOSCAN™, which is a brand of chlorin. Additional photosensitizers include PURLYTIN™ (tin ethyl etiopurpurin) which is available from Miravant (Santa Barbara, Calif.) and VERTEPORFIN™ (Visudyne™) which is a liposomal benzoporphyrin derivative available from QLT Phototherapeutics (British Columbia, Canada; Ciba Vision, Atlanta, Ga.).

[0034] The photosensitizer reagents for use in the methods provided herein include but are not limited to chlorins, bacteriochlorins, phthalocyanines, porphyrins, purpurins, merocyanines, psoralens, benzoporphyrin derivatives (BPD), and porfimer sodium and pro-drugs such as delta-aminolevulinic acid, which can produce photosensitive agents such as protoporlphyrin IX, and other suitable photosensitive compounds including ICG, methylene blue, toluidine blue, texaphyrins, and any other agent that absorbs light in a range of 500 nm to 1100 nm. The photoreactive reagents for use in the methods provided herein include but are not limited to lutetium texaphyrin, marketed as LUTRIN™ (Pharmacyclics, Inc. Sunnyvale, Calif.) or LU-TEX™ (Alcon Laboratories, Fort Worth, Tex.) and bacteriochlorphylls.

[0035] Any of the photosensitizers described above can be used in the methods of the invention. Of course, mixtures of two or more

> photoactive compounds can also be used; however, the effectiveness of the treatment depends on the absorption of light by the photosensitizer so that if mixtures are used, components with similar absorption maxima are preferred.
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> [0036] Methods for activating a sensitizer generally utilize a photoreactive light. As used herein, "photoreactive light" refers to light of sufficient intensity and wavelength to activate the photosensitive agent. For photodynamic therapy, photoreactive light is generally classified as "coherent" light. Coherent light is typically generated from a device commonly known as a laser. However, the present invention encompasses the use of non-coherent photoactivating light as long as the non-coherent light provides the appropriate activating wavelength range for the photosensitizer. As used herein, an "activation wavelength range" is the wavelength range over which the photosensitizer is activated. The photosensitizing agents of the present invention preferably have an absorption spectrum that is within the range of wavelengths between 350 nm and 1200 nm, preferably between about 400 and 900 nm and, most preferably, between 600 and 800 nm.

(underlining emphasis added.) Applicants respectfully submit that contrary to the Office Action, the specification sets out functional characteristics for a photosensitizer as well as approximately thirty (30) specific compounds that can be used as a "photosensitizer". The description by Applicants in the present specification of about 30 photosensitizer compounds is in sharp contrast to the allegations in the Office Action that "As a result, the fact pattern indicates that the artisan was not in possession of the claimed method of use." (see, page 3, line 11-12).

Applicants respectfully request withdrawal of the rejection.

II. REJECTION UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 1-11, 13-18 and 24 stand rejected under 35 U.S.C. §112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards and the invention. Applicants respectfully traverse this rejection with respect to the amended claims.

The Office Action alleges that the term "about" is a relative term that renders the claim indefinite. Applicants respectfully point out that

terms of degree such as "about" are not per se indefinite. The fact that claim language, including terms of degree, may not be precise, does not automatically render the claim indefinite under 35 U.S.C. §112, second paragraph. *Seattle Box Co., v. Industrial Crating & Packing, Inc.*, 731 F.2d 818, 221 USPQ 568 (Fed. Cir. 1984); MPEP §2173.05(b). For example, the term "about" used to define the area of the lower end of a mold as between 25 to "about" 45% of the mold entrance was held to be clear, but flexible. *Ex parte Eastwood*, 163 USPQ 316 (Bd. App. 1968). Similarly, in *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), the court held that a limitation defining the stretch rate of a plastic as "exceeding about 10% per second" is definite because infringement could clearly be assessed through the use of a stopwatch.

Acceptability of the claim language depends on whether one of ordinary skill in the art would understand what is claimed, in light of the specification. When a term of degree is presented in a claim, first a determination is to be made as to whether the specification provides some standard for measuring that degree. MPEP §2173.05(b).

Here, the claims provide that the light is of a dose of greater than about 50j/cm^2. Whether this degree is appropriate is based upon reviewing the specification to provide some standard for measuring that degree (see, *e.g.*, MPEP 2173.05(b)). The specification supports this claim language at, for example, paragraph 40, which reads:

> [0040] The various parameters used for photodynamic therapy in the invention are interrelated. Therefore, the dose of the photosensitizer should be adjusted with respect to other parameters, for example, fluence, irradiance, duration of the light used in photodynamic therapy, and time interval between administration of the dose and the therapeutic irradiation. All of these parameters should be adjusted to produce significant enhancement of destruction of a targeted feeder vessel without significant damage to the eye tissue. The fluence during the irradiating treatment can vary widely, depending on type of tissue, depth of target tissue, and the amount of overlying fluid or blood, but preferably varies from about 50-200 Joules/cm^2. The irradiance typically varies from about 150-900 mW/cm^2, with the range between about 150-600 mW/cm^2 being preferred. However, the present

invention provides for the use of higher irradiances which have the advantage of shortening treatment times and increasing the likelihood effecting a targeted feeder vessel.
…
[0075] The treatment can involve a range of light doses including 50 J/cm^2, 100 J/cm^2, 125 J/cm^2 and 150 J/cm^2, or higher, delivered extrafoveally over 1, 5, 7, 10, 12, 15, 20, 30 or 60 minutes after the introduction of the photosensitizer to the patient. Generally a predetermined drug dose, for example, 6 mg/m^2, is used. As previously noted, the invention encompasses the use of a range of dosages, including those that are higher than we normally be used in convention PDT.

[0076] The size of the area exposed to therapeutic photoactivating light is also variable as long as the target is a feeder vessel associated with vasculature in need of treatment. For example, a laser spot size of 1,000-2,000 microns can be used at the discretion of the physician performing the procedure. of course, the size of the feeder vessel can be used to determine the area of exposure needed to close the vessel. For example, the size of a feeder vessel is generally in the range of 100 to 500 microns. In the present invention, the laser spot size can be smaller because an activating light source is coupled to an imaging device, such as an HRA or HRT. When using higher light doses, the time of light application necessary for achieving the required light dose can be relatively long (166 seconds for 100 J/cm^2, 208 s for 125 J/cm^2 and 249 s for 150 J/cm^2).

[0077] The treatment can be divided in to consecutive treatments that add-up to the needed exposure time. For example, the photoactivating light treatment be stopped every 50-100 sec, or every 50 J/cm^2 delivered, and re-commenced about 30 seconds later. Note that 125 J/cm^2 of light treatment can be interrupted after 2 sets of 83 seconds and completed after the last set of 42 seconds. Once safety parameters have been established for a particular patient, the photoactivating light dose, photosensitizer dosage, photoactivating light exposure time, or number of treatments, can be escalated to affect the closure of a targeted feeder vessel. The following descriptions of dosages and exposure times for performing a method using an apparatus of the invention are exemplary and do not in any limit the invention:

[0078] Vials for injection in clear glass vials of 15 mg. Drug dose of about 6 mg of verteporfin/m^2. Infusion time of about

10 minutes. Light dose of about 50 J/cm^2, 100 J/cm^2, 125 J/cm^2 and 150 J/cM^2. Light administration for about 15 minutes after end of infusion. Light intensity of about 600 mW/cm^2. Laser spot size of about 1,000-2,000 microns.

The specification clearly gives a range that provides a measure of the degree of "about". This is consistent with the MPEP at Section 2173.05(b), "When a term of degree is presented in a claim, first a determination is to be made as to whether the specification provides some standard for measuring that degree." Accordingly, the term "about" is not so undefined as to be indefinite. By proper reference to the specification, the Examiner will note that there is a range provided that sufficient defines the degree encompassed by the claim.

For, at least, the foregoing reasons Applicants believe that this rejection may be properly withdrawn.

Claim 11 stands rejected as unclear because the claim is allegedly broader than the independent claims. Applicants respectfully disagree. Claim 11 is directed to image analysis where as claim 1 uses a high speed scanning laser ophthalmascope. The ophthalmascope is used to obtain images which may be process manually or through automated image analysis. Claim 11 has been amended to indicate that the image analysis is an automated image analysis.

For, at least, the foregoing reasons Applicants believe that this rejection may be properly withdrawn.

Claim 12 is allegedly unclear as it is to a different method of image analysis than the method recited in independent claim 1. Applicants respectfully disagree. Fluorescein angiography is a species/technique that can be used in combination with the high speed scanning laser ophthalmoscope.

For at least the foregoing reasons, Applicants respectfully request withdrawal of this rejection.

Claim 13 stands rejected as allegedly indefinite. Claim 13 has been cancelled thus the rejection is moot with respect to this claims.

III. REJECTION UNDER 35 U.S.C. §103

Claims 1-8, 10-11, 13-17, 24 and 41-42 stands rejected under 35 U.S.C. §103 as allegedly unpatentably over Levy *et al.* (USP 5,798,349), in view of Jampol *et al.* and further in view of Roach (EyeNet Magazine March 2001). Applicants respectfully traverse this rejection.

The eye includes a number of defined areas used in measuring treatment modalities for phototherapies. One of skill in the art will recognize that the term "Extrafoveal" refers to an area that is at least 200 μm from the avascular center of the fovea. The term "Juxtafoveal" refers to an area that is between 1 and 199 μm from the avascular center of the fovea. Accordingly, the treatment of a juxtafoveal region is different than the treatment of an extrafoveal region.

Levy *et al.* (the primary reference) do not teach or suggest (i) topical application of a photosensitizer, (ii) use of a high speed scanning laser ophthalmoscope, (iii) the use of indocyanine green, (iv) the use of non-coherent light, and/or targeting (e.g., identifying and exposing) chorodial neovascularization in the extrafoveal area, or (v) identifying a feeder vessel in an extrafoveal area. In the

The specification describes the importance of identifying and treating a feeder vessel is important in stopping neovascularization in the extrafoveal area. Typically PDT treats neovascularization in the region of vessel growth within the foveal area (NOT the extrafoveal area). Furthermore, PDT used at the time of conception of the present invention was directed to the foveal area using doses below 50 J/cm^2 to prevent damage. Furthermore, PDT used at the time of conception of the present invention did not target feeder vessels in the extrafoveal area. Levy *et al.* do not teach or suggest these important considerations or elements.

To overcome these deficiencies the Office combines Jampol *et al.* with Levy for the alleged teaching of exposing the extrafoveal area to PDT. Jampol *et al.*, however, do not discuss or described identifying a feeder vessel in the extrafoveal area. As described in the present application the importance identifying a feeder layer is important in reducing further neovascularizaiton. "The advantage to treating feeder vessels is the possibility that a large CNV complex can be eliminated by closing a small number of feeder vessels. Further, feeder vessels are generally

localized to an area outside the central portion of the macula (i.e., the vessels are "extra-foveal")." (paragraph [0009] of publication no. 20060258629).

The Examiner alleges that Jampol *et al.* teach ". . .(PDT) with verteporfin is well-known for treating patients with Subfoveal choroidal neovascularization (CNV) and should be considered for the therapy of CNV that is not subfoveal in certain situations such as juxtafoveal and extrafoveal CNV." It appears that the Examiner is referencing a sentence at page 99, last line of first column to second column line 2. This sentence does not mention juxtafoveal or extrafoveal CNV. Furthermore, a more thorough reading of the references does not teach or suggest identifying a feeder vessel in the extrafoveal region. In contrast Jampol *et al.* teach and suggest that juxtafoveal and extrafoveal treatment result in temporary relief but are typically followed by growth or creeping of the scar and delayed degenerative changes leading to visual loss. (See, e.g., page 99, column 2, lines 16-19). This is best explained by the fact that the feeder vessels (as set forth in the pending claims) are NOT identified or targeted by the methods described by Levy *et al.* or Jampol *et al.*

Accordingly, Levy *et al.* in combination Jampol *et al.* fail to teach, suggest or contemplate the claimed invention. Only in hindsight is the importance of the claimed invention identified. The test for obviousness is not what one gleans from the teachings of the application during examination by the Office, but rather what, standing in the shoes of the inventor(s) at the time the invention was conceived would render the invention obvious. As described above, the references and the understanding in the art does not support the piecing together of the invention as suggested by the Office using hindsight. The combination of Levy *et al.* and Jampol *et al.* do not teach and suggest all of the elements of Applicants' claimed invention.

To further attempt to overcome the Levy *et al.* and Jampol *et al.* deficiencies, the Office combined Roach for the alleged teaching the new and sophisticated imaging systems are improving treatment of AMD. Applicants respectfully submit that the provision of a better and fast scope doesn't provides the missing elements of the prior references when combined.

Accordingly, the reference cannot render the claimed invention obvious.

Claim 9 stands rejected under 35 U.S.C. §103 as allegedly unpatentably over Levy *et al.* (USP 5,798,349), in view of Jampol *et al.* and further in view of Roach (EyeNet Magazine March 2001) and further in view of Levy *et al.* (USP 4,920,143). Applicants respectfully traverse this rejection.

Claim 9 is dependent upon claim 1 either directly or indirectly. Each element of the independent claim and any intervening claims is present in claim 9. Levy *et al.*, Jampol *et al.* and Roach are discussed above. These references also fail to teach and suggest topical application of the photosensitizer. Levy *et al.* is combined with the foregoing reference to allegedly teach and suggest topical photosensitizers. However, Levy *et al.* fail to correct the deficiencies identified with respect to Levy et al, Jampol *et al.* and Roach *et al.* and thus does not set forth a prima facie case of obviousness.

Claim 18 stands rejected under 35 U.S.C. §103 as allegedly unpatentably over Levy *et al.* (USP 5,798,349), in view of Jampol *et al.* and further in view of Roach (EyeNet Magazine March 2001) and further in view of LumaCare (press release). Applicants respectfully traverse this rejection.

Claim 18 is dependent upon claim 1 either directly or indirectly. Each element of the independent claim and any intervening claims is present in claim 9. Levy *et al.*, Jampol *et al.* and Roach are discussed above. These references also fail to teach and suggest non-coherent light energy. LumaCare is combined with the foregoing reference to allegedly teach and suggest non-coherent light. However, LumaCare fails to correct the deficiencies identified above and thus does not set forth a prima facie case of obviousness.

Claims 1-8, 10-11, 13-17 and 24 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Sullivan (Jacksonville Medicine) in view of Jampol *et al.* and further in view of Roach (EyeNet Magazine March 2001).

Sullivan does not teach or suggest (i) topical application of a photosensitizer, (ii) use of a high speed scanning laser ophthalmoscope, (iii) the use of indocyanine green, (iv) the use of non-coherent light, and/or (v) photodynamic therapy of a feeder vessel in an extrafoveal region or area. In addition, Sullivan does not teach or

suggest photodynamic therapy using a dose that is about 4x the standard recognized dose of about 12 J/cm^2 (e.g., about 50 J/cm^2, as recited in Applicants' claims). As the Examiner admits, Sullivan does not teach the method for treating an aberrant choridal neovasculature in an extrafoveal area of the eye or the fluence of the photoactivating light.

Furthermore, if the Examiner takes the teachings of the reference being cited as a whole, Sullivan *et al.* teach away from such higher doses indicating that "the benefits of laser treatment are limited because laser photocoagulation damages the viable neurosensory retina. . ." (see, e.g., page 398 of Sullivan *et al.*). Such neurosensory portions of the retina include the foveal area.

To overcome these deficiencies of Sullivan *et al.*, the Office combines Jampol *et al.* for the alleged teaching of exposing the extrafoveal area to PDT. Jampol *et al.*, however, do not discuss or describe identifying a feeder vessel in the extrafoveal area. As described in the present application the importance identifying a feeder layer is important in reducing further neovascularizaiton. "The advantage to treating feeder vessels is the possibility that a large CNV complex can be eliminated by closing a small number of feeder vessels. Further, feeder vessels are generally localized to an area outside the central portion of the macula (i.e., the vessels are "extra-foveal")." (paragraph [0009] of publication no. 20060258629).

Jampol *et al.* as well as Sullivan *et al.* do not teach or suggest identifying a feeder vessel in the extrafoveal region. Jampol *et al.* teach and suggest that juxtafoveal and extrafoveal treatment result in temporary relief but are typically followed by growth or creeping of the scar and delayed degenerative changes leading to visual loss. (See, e.g., page 99, column 2, lines 16-19). This is best explained by the fact that the feeder vessels (as set forth in the pending claims) are NOT identified or targeted by the methods described by Sullivan *et al.* or Jampol *et al.*

Accordingly, Sullivan *et al.* in combination Jampol *et al.* fail to teach, suggest or contemplate the claimed invention. Only in hindsight is the importance of the claimed invention identified. The combination of Sullivan *et al.* and Jampol *et al.* do not teach and suggest all of the elements of Applicants' claimed invention.

To further attempt to overcome the Sullivan *et al.* and Jampol *et al.* deficiencies, the Office combines Roach for the alleged teaching the new and sophisticated imaging systems are improving treatment of AMD. Applicants respectfully submit that the provision of a better and fast scope does not provide the missing elements of the prior references when combined.

Accordingly, the reference cannot render the claimed invention obvious.

Claim 9 stands rejected under 35 U.S.C. §103 as allegedly unpatentably over Sullivan *et al.*, in view of Jampol *et al.* and further in view of Roach (EyeNet Magazine March 2001) and further in view of Levy *et al.* (USP 4,620,143). Applicants respectfully traverse this rejection.

Claim 9 is dependent upon claim 1 either directly or indirectly. Each element of the independent claim and any intervening claims is present in claim 9. Sullivan *et al.*, Jampol *et al.* and Roach are discussed above. These references also fail to teach and suggest topical application of the photosensitizer. Levy *et al.* is combined with the foregoing reference to allegedly teach and suggest topical photosensitizers. However, Levy *et al.* fail to correct the deficiencies identified with respect to Sullivan et al, Jampol *et al.* and Roach *et al.* and thus does not set forth a prima facie case of obviousness.

Claim 18 stands rejected under 35 U.S.C. §103 as allegedly unpatentably over Sullivan *et al.* in view of Jampol *et al.* and further in view of Roach (EyeNet Magazine March 2001) and further in view of LumaCare (press release). Applicants respectfully traverse this rejection.

Claim 18 is dependent upon claim 1 either directly or indirectly. Each element of the independent claim and any intervening claims is present in claim 9. Sullivan *et al.*, Jampol *et al.* and Roach are discussed above. These references also fail to teach and suggest non-coherent light energy. LumaCare is combined with the foregoing reference to allegedly teach and suggest non-coherent light. However, LumaCare fails to correct the deficiencies identified above and thus does not set forth a prima facie case of obviousness.

Claims 41-42 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Sullivan *et al.* in view of Jampol *et al.* in view of Roach and further in view of Miller *et al.* Applicants respectfully traverse this rejection.

Sullivan *et al.*, Jampol *et al.*, and Roach *et al.* have been discussed above. Miller *et al.* is combined with the foregoing to allegedly overcome the deficiency related to the fluence of the photoactivating light. Applicants respectfully submit that even if Miller *et al.* overcame the deficiencies of the fluence, the reference still does not overcome the numerous other deficiencies as set forth above with regarding to Sullivan *et al.*, Jampol *et al.* and Roach *et al.*

For at least the foregoing, the Applicant submits that the claimed invention is patentable and request reconsideration and notice of such allowable subject matter.

The Director is authorized to charge any required fee or credit any overpayment to Deposit Account Number 50-4586, please reference the attorney docket number above.

The Examiner is invited to contact the undersigned at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted,

GAVRILOVICH, DODD & LINDSEY LLP

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By: /Joseph R. Baker, Jr./
Joseph R. Baker, Jr.
Registration No. 40,900

4660 La Jolla Village Drive, Suite 750
San Diego, California 92122
(858) 458-3607 (Main)
(858) 458-9986 (Fax)